Original Research Article

Health related quality of life in children and adolescents with sickle cell disease in central India

Nikita Suresh Gupta*, Chandrakant M. Bokade

Department of Pediatrics, Government Medical College, Nagpur, Maharashtra, India

Received: 21 January 2022

Revised: 07 February 2022

Accepted: 09 February 2022

*Correspondence:

Dr. Nikita Suresh Gupta,

E-mail: nikitagupta178@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Sickle cell disease (SCD) is major health problem in central India. This is a single centre study conducted to assess the health-related quality of life (HRQOL) in children and adolescent with homozygous (SS pattern) and heterozygous (AS pattern) SCD with respect to healthy children.

Methods: This is a case control study conducted in a tertiary care hospital. Study group included total of 150 children and adolescents with SS pattern and AS pattern. HRQOL of the children in study group was compared with demographically matched 100 healthy children in comparison group. WHO-QOL BREF questionnaire was administered to both the groups to measure their HRQOL in various domains. Multivariable linear regression was used to account for socio-demographic factors influencing HRQOL.

Results: The WHO-QOL BREF scores of children with SS pattern were significantly lower than those obtained in the AS pattern and healthy children ($p < 0.001$) in all studied domains (physical, psychological, social and environmental). The domain scores of HRQOL in children with AS pattern didn't differ significantly as compared to healthy children. Results also highlighted that along with severity of disease, various demographic characteristics like age, gender, locality and socioeconomic status had significant impact on various domains of HRQOL.

Conclusions: SCD has detrimental effect on HRQOL of growing children and adolescent that is compounded by various demographic and socio-environmental factors in a developing country.

Keywords: Quality of life, Sickle cell, Child, Adolescent

INTRODUCTION

Sickle cell disease (SCD) is a hemoglobinopathy inherited due to single DNA mutation in β globin gene. It is prevalent worldwide but more common in Sub-Saharan Africa, Saudi Arabia and central India. India ranks second in terms of global SCD burden.¹ The distribution of sickle cell gene is uneven in Indian population geographically and socially. It is predominantly found in socioeconomically marginalized tribal population residing in villages. The severity of disease also varies among various regions in India with severe phenotype being reported in children of central India.²

Morbidity in children's with SCD is attributed to frequent pain, vaso-occlusive crisis, growth faltering, organ system dysfunction, strokes, frequent hospitalizations and blood transfusions. Children with SCD often have emotional internalizing disturbances, poor social skills, lower school attendance due to sickness absenteeism and suboptimal school performance. SCD impose prodigious psychosocial burden affecting physical, psychological, social and occupational well-being. Thus, health related quality of life (HRQOL) is an important parameter to assess well-being in children with SCD.^{3,4} HRQOL is a valuable outcome reported by patients that emphasizes patient's outlook of his or her experience rather than analyzing

objective parameter of health. It facilitates us to analyze the impact of disease identify issues requiring intervention, comparison of therapies, and allocation of resources.⁵ Hence the measurement of HRQOL in patients suffering from chronic illnesses has gained importance. Poor outcome of HRQOL has been reported for diseases like chronic kidney disease, asthma, congenital heart disease, HIV etc. McClish et al found that the HRQOL outcome in adults with SCD were comparable to various chronic diseases.⁶

The Vidarbha region of central India, where our tertiary care and referral center is located has frequency of HbS gene 0-14% varying among tribal and non-tribal population and different ethnic groups.⁷ We have a sickle cell clinic where comprehensive health care is provided to patients with SCD both on outpatient and inpatient basis. Thus, this study was conducted with aim to: 1. Evaluate HRQOL in children with SS pattern and AS pattern with respect to normal children. 2. Assess impact of disease severity on quality of life in children with homozygous SCD and 3. Study the correlation of HRQOL with demographic characteristics.

METHOD

This is an analytical cross-sectional study conducted in Indira Gandhi government medical college, Nagpur, in central India from October 2015 to October 2017. We enrolled 150 children aged 8-18 years in study group, out of which 100 children had homozygous SCD (SS pattern) and 50 had heterozygous SCD (AS pattern). 100 healthy children were also enrolled constituting comparison group. Study group included all diagnosed cases of SS pattern and AS pattern SCD attending sickle cell clinic or admitted in pediatric ward. Subjects with other hemolytic anemia or co-morbidities like HIV and hepatitis B were excluded. Comparison group included children attending OPD clinic for minor illnesses and their healthy siblings with matching demographic characteristics. Children having family history of SCD and other hemoglobinopathy were excluded. A written informed consent was obtained from parents or guardians after explaining to them the nature of the study. Ethical clearance for conducting the study was obtained from the institutional ethics committee.

A detailed demographic, socioeconomic and clinical history was obtained. As no definite criterion for grading severity of SCD is available we defined severe SCD as presence of any one of the following; ≥ 3 episode of vaso-occlusive crisis requiring hospitalization per year, ≥ 3 blood transfusions per year, single episode of acute chest syndrome or stroke and avascular necrosis.⁸ The socioeconomic status of individuals was classified into five classes as per modified Kuppuswamy scale. WHO-QOL BREF was administered for the assessment of health-related quality of life. The information obtained during the study was kept

confidential and to avoid influence from family members the interviewer emphasized that the child should be alone in the room while attempting questionnaire.

Instrument

The world health organization quality of life (WHO-QOL) instrument WHO-QOL BREF is cross-culturally validated generic instruments available in 30 languages, including Hindi and Tamil. It has shown good psychometric properties in determining HRQOL, in patients with SCD and has been validated in Indian adolescents in local languages with high internal consistency and good predictive validity.⁴ It has been proved to be comparable or even better than other QOL instruments for Indian adolescents.⁹ We used culturally modified translated version of WHO-QOL BREF scale in regional languages of Hindi and Marathi. WHOQOL-BREF is abbreviated version of WHOQOL-100 consisting of 26 items. It consists of two items from general health and overall QOL and, one item each from remaining 24 facets in the WHOQOL-100. These facets are scored in four domains: Physical (7 items), psychological (6 items), social relationships (3 items) and environment (8 items). Responses to questions in various domains are presented as a Likert scale of five points from 1 (very bad) to 5 (very good QOL). The comparison between domains containing unequal number of items was made by transforming scores on a scale of 0-100.^{10,11}

Statistical analysis

Continuous variables like age were presented as a mean $\pm$ standard deviation and categorical variables were expressed in frequency and percentages. Continuous variables were compared between different domains of quality of life by performing independent T test. Domain scores in three groups were compared by performing one way ANOVA test. Multiple comparisons were carried out by BONFERRONI TEST. All the test was two sided. $P < 0.05$ was considered statistical significance. Statistical software STATA version 14.0 was used for data analysis.

RESULTS

The mean age of children with SS pattern and AS pattern enrolled in the study was 12.34 ± 2.86 and 12.5 ± 2.82 years respectively. In order to assess the influence of age in HRQOL the study and comparison group were divided into 3 groups 8-11 years, 12-14 years and 15-18 year. 57 cases were male and 43 were females in SS pattern group. In AS pattern group there were 30 male and 20 female out of 50 cases enrolled (Table 1). Majority of children belonged to lower middle socioeconomic group. Locality distribution showed that 58% were from rural area whereas 42% were from urban area. There was

significant difference ($p<0.001$) in mean age at diagnosis in children with SS pattern (2.94 ± 1.46 years) and AS pattern (4.152 ± 1.90 years). Out of 100 children with homozygous SCD, 32 had severe disease as per the criteria.

In global question one, the study population with SS pattern rated quality of life good or very good in 55%, followed by neither good nor bad in 26% and bad or very bad in 15%. In cases with AS pattern and 78% rated it positively, 14% rated neither good nor bad and 8% rated negatively. In global question two, 48.3% children with SS pattern were satisfied or very pleased with their health, followed by 28.4% neither satisfied nor dissatisfied and 23.3% dissatisfied or very dissatisfied. 84% children with AS pattern were satisfied or very satisfied and 16% were neither satisfied nor dissatisfied

Children with SS pattern scored significantly less in all domains of WHO-QOL BREF scale (Table 2) as

compared to children with AS pattern and healthy children with significant $p<0.001$ in each domain. Environmental domain had lowest score of 53.13 ± 9.24 . On the other hand, children with AS pattern did not show statistically significant difference in domain score as compared to healthy children. In children with homozygous SCD having severe disease all the four domains of HRQOL ($p<0.001$) with were markedly affected as compared to those having non severe disease (Table 3).

Effect of age on domain scores of WHO-QOL BREF revealed statistically significant decrease in all domain scores with increasing age. Female gender had significant low score in physical and social domains with $p<0.001$ and 0.029 respectively compared to male gender. Lower socioeconomic status adversely affected physical health ($p=0.016$) sparing other domains of HRQOL. The children from rural locality scored low in environmental domain ($p=0.007$).

Table 1: Socio-demographic characteristics of study and comparison group.

Socio-demographic characteristic	SS group	AS group	Comparison group	P value
Mean age (Years)	12.34 $\pm$ 2.86	12.5 $\pm$ 2.82	12.61 $\pm$ 3.02	0.8667
Sex				
Female	43	20	45	0.825
Male	57	30	55	
Locality				
Urban	42	27	46	0.381
Rural	58	23	54	
Socio-economic class				
Upper	6	3	4	0.837
Upper middle	8	3	10	
Upper lower	30	13	26	
Lower middle	46	27	49	
Lower	10	6	11	

Table 2: HRQOL in study group and comparison group.

HRQOL domain	SS pattern group, (n=100)	AS pattern group, (n=50)	Comparison group, (n=100)	P value		
				SS vs comparison	SS vs AS	AS vs comparison
Physical	56.32 $\pm$ 10.60	70.4 $\pm$ 10.11	84.0 $\pm$ 7.19	<0.001	<0.001	0.078
Psychological	69.37 $\pm$ 9.32	75.72 $\pm$ 6.13	80.15 $\pm$ 6.78	<0.001	<0.001	0.219
Social	76.29 $\pm$ 16.65	77.38 $\pm$ 8.51	89.76 $\pm$ 9.92	<0.001	<0.001	0.272
Environmental	53.13 $\pm$ 9.24	59.96 $\pm$ 8.55	74.24 $\pm$ 7.52	<0.001	<0.001	0.362

Table 3: Relation of severity of disease and HRQOL in children with SS pattern.

Domains of HRQOL	Severe disease in SS pattern, (n=100)		P value
	Yes, (n=32)	No, (n=78)	
Physical	48.09 $\pm$ 11.06	60.19 $\pm$ 7.88	<0.001
Psychological	61.34 $\pm$ 10.68	73.14 $\pm$ 5.51	<0.001
Social	61.75 $\pm$ 16.36	83.13 $\pm$ 11.74	<0.001
Environmental	48.56 $\pm$ 8.86	55.54 $\pm$ 8.60	<0.001

Table 4: Relation of socio-demographic characteristic with HRQOL in children with SS pattern.

No. of cases		Physical	Psychological	Social	Environmental
Age (years)					
8-11	40	58.07±11.54	69.72±8.73	79.27±16.92	55.52±9.56
12-14	36	52.52±6.76	64.86±8.22	76.58±15.34	52.83±9.37
15-18	24	49.75±10.81	61.91±8.37	67.33±15.39	47.79±7.92
P value	(T=100)	0.0035	0.0015	0.0160	0.0061
Gender					
Male	57	57.54±10.14	66.26±8.70	78.56±15.79	54.63±10.44
Female	43	49.48±8.89	63.37±7.34	71.30±16.77	50.97±7.35
P value	(T=100)	0.0001	0.0821	0.0290	0.0533
Locality					
Rural	58	52.96±9.56	64.17±8.15	74.72±16.53	50.93±9.60
Urban	42	55.61±11.34	66.19±8.29	76.42±16.69	56.0±8.31
P value	(T=100)	0.2087	0.2282	0.6135	0.0070
Socioeconomic status					
Upper	6	61.5±10.85	66.0±5.01	65.83±6.58	55.16±10.70
Upper middle	8	58.75±7.55	68.12±7.69	86.0±11.0	57.87±8.16
Upper lower	30	56.96±10.37	64.6±8.38	78.4±16.66	52.36±10.96
Lower middle	46	51.17±10.05	64.73±8.97	73.69±17.28	53.32±8.72
Lower	10	50.6±9.08	64.5±6.77	71.9±16.78	48.8±6.19
P value	(T=100)	0.0166	0.8508	0.1225	0.3260

*T-total no of children in SS pattern group

DISCUSSION

The domain of health-related quality of life was relatively unexplored component of health care but now it is being increasingly recognized in developing countries. The high prevalence of SCD in central India warrants the estimation of HRQOL in these children that will help us understand various physical, social, psychological and economic issues encountered by children and their families. Ample studies have been carried out globally to evaluate influence of various factors such as role of socio-demographics, disease severity and the presence of complications on HRQOL in SCD patients.¹²⁻¹⁵

While similar literature from India is scarce.¹⁶ To our knowledge this is the largest study reported from central India addressing the concerns of health-related quality of life in children and adolescents suffering from SCD. The mean age of detection in patients with SS pattern was significantly lower than patients with AS pattern in our study. As there is lack of national neonatal screening program for SCD, children are diagnosed only when they become symptomatic.¹⁷

The response of global questions 1 and 2 based on perception of quality of life and health was overall positive. Although children were sick, most of them were satisfied about their quality of life and health status.

In children with SS pattern, all four domains of WHO-QOL BREF scale were significantly affected

with lowest score in environmental domain followed by physical, psychological and social domain respectively as compared to healthy children. The worst outcome in environmental domain in our study is paradoxical to most of the previously reported studies that demonstrated physical domain to be worst affected.¹⁸⁻²⁰ It was also found that social domain relatively scored better as compared to others.

The poor environmental health witnessed may be due to the fact that majority of children belonged to ethnic minority residing in villages. They suffer from dual challenges of, their chronic disease state and environment of social discrimination, poor housing facilities and difficult access to health services. They need to have frequent visits to hospitals due to disease complications with expenditure of money and resources. Sarah et al highlighted various modifiable socio-environmental factors in children with SCD that may help to improve their cognitive and behavioral functioning.²¹ Rural locality was also found to have adverse influence on environmental domain as compared to urban locality in SS group. Besides aforementioned factors, coping styles and perception of illness may also lead to urban-rural differences in patients with SCD. The impact of locality on HRQOL has been accounted by very few studies in past.²²

The impact on physical domain can be explained by frequent episode of vaso-occlusive crisis, fatigue and reduced working capacity which interferes with their ability to participate in sports activities and absenteeism from school. Psychological domain of children with SCD was affected due to various internalizing and

externalizing behavioral problems such as anxiety, low self-esteem and depression. It has also been suggested by Unal et al that severity of disease is strong predictor of poor psychological outcome in children whereas Sehlo et al showed that increased level of parent support was significantly associated with decreased depressive symptoms and better quality of life in these children.^{23,24}

Children and adolescents with SCD showed significantly low social competence, that may be attributed to limited peer contact, delayed physical maturation and functional impairment due to disease, alike reported by former studies.²⁵ On the contrary Noll et al demonstrated stable social functioning in children with SCD over time.²⁶ Although low but relatively better scores in social domain may be due to the support these children get from their families and society considering their chronic morbid state. The development of coping skills to stressors in life, help psychosocial adaptation in children with SCD and their families.²⁷

In this study we found statistically significant decrease in all domain scores with increasing age. Negative influence of increasing age was also shown by Palermo et al and Panepinto et al adolescents with SCD face more problems in adaptation as compared to their younger counterparts, such as poor self-esteem and problems with peer relation.^{15,28} They experience abnormal sexual and physical development, in the form of delayed growth and puberty, short stature and priapism that adds to more concerns in growing patient.

In our study HRQOL was also affected by gender difference with females scoring low in physical and social domain. Monhen Amr et al reported lower scores in physical functioning in adolescent girls but scores in social and emotional well-being were high as compared to healthy peers.¹³ Whereas others study found no gender difference.²⁹

This study also reveals negative influence of lower socioeconomic status on physical domain in patients with SCD. Many past researches have also highlighted negative influence of lower socioeconomic status on HRQOL in children with SCD.³⁰ Although in a developing country this factor is indispensable and beyond the arena of health care provider, rate of complications can be reduced to minimize economic burden on families.

Four domain scores of WHO-QOL BREF scale in AS pattern group were significantly better, as that of SS pattern. In comparison to healthy children their scores were numerically low but failed to show statistical significance. Most of the patients of AS pattern are expected to be asymptomatic as they experience occasional pain crisis, require less hospitalization or blood transfusions as compared to SS pattern. Thus, in terms of HRQOL the life of patients with heterozygous

disease is much better than of homozygous and is comparable to healthy children. There is hardly any study highlighting HRQOL patient with sickle cell trait.

The strength of our study is larger number of children in study group as compared to other studies reported from central India. The design of study is case control in which the comparison of HRQOL with healthy peers has been done. Although not disease specific but a well validated scale in Indian population and in patients with SCD was implemented to assess HRQOL.

However, there were few limitations in study. The difference in HRQOL of outpatients and inpatients was not considered separately that could affect the patient reported outcome. We did not categorize children on grounds of treatment (chronic transfusion therapy or hydroxyurea) they were receiving that might influence their HRQOL.

CONCLUSION

This study concluded that, quality of life in children with homozygous pattern of SCD is severely affected as compared to normal healthy children in all domains. Along with severity of SCD, various demographic characteristics like age, gender, locality, socioeconomic status also has negative influence on HRQOL. Children with sickle cell trait have milder form disease with their HRQOL comparable to healthy children.

Recommendations

Assessment of HRQOL should be an integral part in the management of children with SCD along with treating pain and disease related complications in order to improve their quality of life.

There is need of interventional studies particularly in developing countries to improve HRQOL in children with SCD in future prospect.

ACKNOWLEDGEMENTS

Author would like to thanks to department of pediatrics, government medical college, Nagpur.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Hockham C, Bhatt S, Colah R, Mukherjee MB, Penman BS, Gupta S et al. The spatial epidemiology of sickle-cell anaemia in India. *Sci Rep.* 2018;8(1):17685.
2. Jain D, Italia K, Sarathi V, Ghoshand K, Colah R. Sickle cell anemia from central India: a retrospective

- analysis. *Indian Pediatr.* 2012;49(11):911-3.
3. Wrotniak B, Schall J, Brault M, Balmer D, Stallings V. Health-Related Quality of Life in Children with Sickle Cell Disease Using the Child Health Questionnaire. *J Pediatric Health Care.* 2014;28(1):14-22.
4. Asnani MR, Lipps GE, Reid ME. Utility of WHOQOL-BREF in measuring quality of life in sickle cell disease. *Health Qual Life Outcomes.* 2009;7:75.
5. Cella DF. Quality of life: concepts and definition. *J Pain Symptom Manage.* 1994;9(3):186-92.
6. Donna M, Lynne P, Victor B, John R, John A, James L et al. Health-related quality of life in sickle cell patients: The PiSCES project. *Health Qual Life Outcomes.* 2005;3:50.
7. Deore UA, Zade SB. Epidemiology of sickle cell disorder: The urban scenario in Maharashtra, India. *Int J Public Health Epidemiol.* 2013;2(5):101-7.
8. Panepinto J, Pajewski N, Foerster L, Sabnis S, Hoffmann R. Impact of family income and sickle cell disease on the health-related quality of life of children. *Quality Life Res.* 2008;18(1):5-13.
9. Agnihotri K, Awasthi S, Chandra H, Singh U, Thakur S. Validation of WHO QOLBREF instrument in Indian adolescents. *Indian J Pediatr.* 2010;77:381-6.
10. WHO, WHOQOL-BREF: introduction, administration, scoring and generic version of the assessment: field trial version. 1996. Available at: <https://apps.who.int/iris/handle/10665/63529>. Accessed on 2 January 2022.
11. Skevington S, Lotfy M, O'Connell K. The World Health Organization's WHOQOL-BREF quality of life assessment: Psychometric properties and results of the international field trial. A Report from the WHOQOL Group. *Quality Life Res.* 2004;13(2):299-310.
12. Dale JC, Cochran CJ, Roy L, Jernigan E, Buchanan GR. Health-related quality of life in children and adolescents with sickle cell disease. *J Pediatr Health Care.* 2011;25(4):208-15.
13. Abdel-Monhem Amr M, Tawfik AT, Al-Omair AO. Health related quality of life among adolescents with sickle cell disease in Saudi Arabia. *Pan Afr Med J.* 2011;8:10.
14. Julie P, Kerry O, Michael D, Loberiza LF, Scott JP. Health-related quality of life in children with sickle cell disease: child and parent perception. *Br J Haematol.* 2005;130(3):437-44.
15. Al Jaouni SK, Al Muhayawi MS, Halawa TF, Al Mehayawi MS. Treatment adherence and quality of life outcomes in patients with sickle cell disease. *Saudi Med J.* 2013;34(3):261-5.
16. Bhagat VM, Baviskar SR, Muddey AB, Goyal RC. Poor health related quality of life among patients of sickle cell disease. *Indian J Palliat Care.* 2014;20(2):107-11.
17. Colah RB, Mehta P, Mukherjee MB. Newborn Screening for Sickle Cell Disease: Indian Experience. *Int J Neonatal Screen.* 2018;4(4):31.
18. Hijmans CT, Fijnvandraat K, Oosterlaan J, Heijboer H, Peters M, Grootenhuys MA. Double disadvantage: a case control study on health-related quality of life in children with sickle cell disease. *Health Qual Life Outcomes.* 2010;8:121.
19. Barakat LP, Patterson CA, Daniel LC, Dampier C. Quality of life among adolescents with sickle cell disease: mediation of pain by internalizing symptoms and parenting stress. *Health Qual Life Outcomes.* 2008;6:60.
20. Dampier C, Lieff S, LeBeau P, Rhee S, McMurray M, Rogers Z et al. Health-related quality of life in children with sickle cell disease: A report from the comprehensive sickle cell centers clinical trial consortium. *Pediatr Blood Cancer* 2010;55:485-94.
21. Bills SE, Schatz J, Hardy SJ, Reinman L. Social-environmental factors and cognitive and behavioral functioning in pediatric sickle cell disease. *Child Neuropsychol.* 2020;26(1):83-99.
22. Telfair J, Haque A, Etienne M, Tang S, Strasser S. Rural/urban differences in access to and utilization of services among people in Alabama with sickle cell disease. *Public Health Rep.* 2003;118:27-36.
23. Unal S, Toros F, Kütük MÖ, Uyaniker MG. Evaluation of the psychological problems in children with sickle cell anemia and their families. *Pediatr Hematol Oncol.* 2011;28(4):321-8.
24. Sehlo MG, Kamfar HZ. Depression and quality of life in children with sickle cell disease: the effect of social support. *BMC Psychiatry.* 2015;15:78.
25. Rodrigue JR, Streisand R, Banko C, Kedar A, Pitel PA. Social functioning, peer relations, and internalizing and externalizing problems among youths with sickle cell disease. *Children's Health Care.* 1996;25:37-52.
26. Noll RB, Kiska R, Reiter-Purtill J, Gerhardt CA, Vannatta K. A controlled, longitudinal study of the social functioning of youth with sickle cell disease. *Pediatrics.* 2010;125:e1453-9.
27. Barbarin OA, Christian M. The Social and Cultural Context of Coping with Sickle Cell Disease: I. A Review of Biomedical and Psychosocial Issues. *J Black Psychol.* 1999;25:277-93.
28. Palermo TM, Schwartz L, Drotar D, McGowan K. Parental report of health-related quality of life in children with sickle cell disease. *J Behav Med.* 2002;25(3):269-83.
29. Fuggle P, Shand PA, Gill LJ, Davies SC. Pain, quality of life, and coping in sickle cell disease. *Arch Dis Child.* 1996;75(3):199-203.
30. Didsbury MS, Kim S, Medway MM. Socio-economic status and quality of life in children with chronic disease: A systematic review. *J Paediatr Child Health.* 2016;52(12):1062-9.

Cite this article as: Gupta NS, Bokade CM. Health related quality of life in children and adolescents with sickle cell disease in central India. *Int J Contemp Pediatr* 2022;9:268-73.